

CHEMICAL HERITAGE FOUNDATION

MIGUEL ANGEL ONDETTI

Transcript of an Interview
Conducted by

James J. Bohning

at

Princeton, New Jersey

on

12 January 1995

(With Subsequent Corrections and Additions)

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MIGUEL ANGEL ONDETTI

1930 Born in Buenos Aires, Argentina, on 14 May

Education

1955 Licentiate, chemistry, University of Buenos Aires
1957 Ph.D., organic chemistry, University of Buenos Aires

Professional Experience

1948-1957 Bookkeeper, Department of Energy, Argentina Government
1957-1960 Professor, Catholic Institute for Teachers
1957-1960 Instructor, University of Buenos Aires

1957-1960 The Squibb Institute for Medical Research, Argentina
Senior Research Chemist

1960-1966 The Squibb Institute for Medical Research, New Jersey
Senior Research Chemist
1966-1973 Research Group Leader, Peptide Synthesis
1973-1976 Section Head, Peptides, Steroids, and Antibiotic Research
1976-1980 Director, Department of Biological Chemistry
1980-1981 Associate Director, Chemical and Microbiological Research
1981-1983 Vice President, Basic Research
1984-1989 Vice President of Research, Cardiopulmonary Diseases
1989-1990 Senior Vice President of Research, Cardiovascular Diseases
1990-1991 Senior Vice President, Cardiovascular and Metabolic Diseases
1991 Retired

Honors

1981 Alfred Burger Award in Medicinal Chemistry, American Chemical Society
1983 Thomas Alva Edison Patent Award, Research and Development Council,
New Jersey
1983 Ciba Award for Hypertension Research, American Heart Association,
Council on High Blood Pressure Research
1986 Chairman's Edward Robinson Squibb Award, E. R. Squibb & Sons, Inc.
1988 Award for Contributions to Medical Science, Pharmaceutical Manufacturers
Association and National Health Council
1988 Inventor of the Year Award, New Jersey Inventors Congress
1991 Perkin Medal, Society of Chemical Industry, American Section
1991 Warren Alpert Foundation Prize, Harvard Medical School
1992 Award for Creative Invention, American Chemical Society
1992 Herman Bloch Award for Scientific Excellence in Industry, University of
Chicago

ABSTRACT

Miguel A. Ondetti begins this interview by describing his parents' immigrant background and work in Argentina, early interests in chemistry, and education at vocational school in Buenos Aires. Upon high school graduation, Ondetti began work as a bookkeeper, continuing studies at night to meet university entrance requirements. He began chemistry coursework at the University of Buenos Aires while supporting himself with accounting work for the government. Here he describes his broad training in chemistry, Argentina's political climate, and his Ph.D. scholarship and carbohydrates research for V. Deulofeu at The Squibb Institute. Upon graduation in 1957, Ondetti explored other opportunities before accepting a position with Squibb's alkaloid isolation group, where he remained until 1960, when after much consideration he accepted a job with Squibb, New Jersey. In New Jersey, Ondetti worked in the peptide chemistry group, synthesizing the nonapeptide bradykinin under M. Bodanszky, with whom he co-wrote *Peptide Synthesis*. He discusses adjusting to life and work in the U.S., and his advancement in the peptide synthesis field and promotion to group head when Bodanszky pursued a career in academia. Ondetti was part of a group effort to synthesize gastrointestinal hormones, particularly secretin, a peptide amide that stimulates the pancreas to secrete bicarbonate and water. While Bodanszky pursued stepwise synthesis of the peptide, Ondetti worked with E. Sabo on fragment condensation approach was used to obtain synthetic secretin for clinical studies, the results of which discouraged further development. Next Ondetti worked with Sabo to synthesize cholecystokinin, which stimulates contraction of the gall bladder and secretion of enzymes from the pancreas. Here he describes problems with the synthetic peptide's development, and its eventual use as a diagnostic agent; also discussed is the importance of his relationships with Sabo and Z. Horovitz. In 1967, A. D. Welch became Squibb's president, and changes in company research agendas led Ondetti to work on peptidase inhibitors. Ondetti describes acquiring venom for isolation of enzyme inhibitors, isolating phospholipase inhibitor, and learning to isolate and sequence peptides in competition with researchers at Brookhaven National Laboratories. In 1973, for practical reasons, Squibb's angiotensin converting enzyme [ACE] inhibitor work officially ended, but Ondetti's interest in the subject continued; prompted by discoveries of L. D. Byers and R. Wolfenden and interactions with D. Cushman, Ondetti decided to pursue synthesis of succinyl-L-proline, which was found to potentiate the contractile activity; after continued research, this work evolved into captopril. Here Ondetti describes human trials of this drug, problems with FDA approval, the effectiveness of captopril for hypertension treatment, and follow-up research leading to new therapeutic agents. The interview closes with Ondetti's reflections on the fields of chemistry and pharmaceutical research, and his own career; highlighted are notions of success and rewards, collaboration between industry and academia, rational drug design, and leadership.

INTERVIEWER

James J. Bohning is Professor of Chemistry Emeritus at Wilkes University, where he was a faculty member from 1959 to 1990. He served there as chemistry department chair from 1970 to 1986 and environmental science department chair from 1987 to 1990. He was chair of the American Chemical Society's Division of the History of Chemistry in 1986, received the Division's outstanding paper award in 1989, and presented more than twenty-five papers before the Division at national meetings of the Society. He has been on the advisory committee of the Society's National Historic Chemical Landmarks committee since its inception in 1992. He developed the oral history program of the Chemical Heritage Foundation beginning in 1985, and was the Foundation's Director of Oral History from 1990 to 1995. He currently writes for the American Chemical Society News Service.

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